
Effects of rupatadine vs placebo on allergen-induced symptoms in patients exposed to aeroallergens in the Vienna Challenge Chamber

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Background: Rupatadine is a novel compound with potent dual antihistamine and platelet-activating factor antagonist activities and no sedative effects.

Objective: To evaluate the efficacy of rupatadine, 10 mg once daily, and placebo on allergen-induced symptoms (including nasal congestion), nasal airflow, nasal secretion, and subjective tolerability in response to grass pollen in a controlled allergen-exposure chamber.

Methods: In a randomized, double-blind, placebo-controlled, crossover trial, 45 patients with a history of seasonal allergic rhinitis received rupatadine or placebo every morning for 8 days in 2 different periods separated by a 14-day washout interval. On day 8 of each crossover period, patients underwent a 6-hour allergen exposure in the Vienna Challenge Chamber, where a constant and homogeneous concentration of aeroallergens was maintained. Subjective and objective assessments were performed online during the exposure.

Results: Subjective single and composite nasal and nonnasal symptoms were consistently less severe with rupatadine use than with placebo use starting from the first evaluation at 15 minutes to the end of the 6-hour Vienna Challenge Chamber challenge, with the most significant effects seen for nasal rhinorrhea, nasal itching, sneezing attacks, and total nasal symptoms ($P < .001$ for all). All the other symptoms (including nasal congestion, $P \leq .005$) were also significantly reduced with active treatment compared with placebo use. Mean secretion weights and overall feeling of complaint were significantly lower with rupatadine therapy than with placebo use ($P \leq .001$). Overall, rupatadine treatment was well tolerated.

Conclusion: Rupatadine treatment is effective and well tolerated in patients with allergen-induced symptoms exposed to aeroallergens in a controlled exposure chamber.

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INTRODUCTION

Allergic rhinitis (AR) is a major health concern that affects 1 in 5 people worldwide and is a significant cause of increased morbidity.^{1–3} Until recently, AR was classified as either seasonal, for which the primary cause is pollen (and, therefore, it is related to the pollen period), or perennial, which is caused by various allergens, such as dust mites, mold spores, and animal danders. Because this subdivision was not entirely satisfactory, AR has been reclassified according to the chronicity of symptoms (intermittent or persistent) and its relative severity (mild, moderate, or severe).^{4–6} In the present study, however, the term *seasonal AR* (SAR) was kept in relation to the AR history of the patients participating in the study because clinical data, such as duration of symptoms and

quality of life, were not available to allow the assumption that SAR and intermittent AR were interchangeable terms.

The major symptoms of AR include rhinorrhea, nasal obstruction, nasal itching, and sneezing. The molecular and cellular mechanisms that mediate the allergic inflammatory cascade involve multiple mediators, cell types, and pathways. The initial response by mast cells and basophils to allergens triggers degranulation and the release of preformed inflammatory mediators, primarily histamine, which is important to the early-phase response. Subsequently, synthesis and release of lipid mediators and cytokines occur, which may contribute to the late-phase response and chronic allergic inflammation.^{7,8} Platelet-activating factor is also an important mediator of AR, and its biological properties include vasodilation and a vascular permeability increase that may contribute to the appearance of rhinorrhea and nasal congestion.^{9–15} Rupatadine is a new potent second-generation antihistamine with a high affinity for H₁ receptors and potent platelet-activating factor antagonist activity^{16–20} characterized by the rapid onset of action and long-lasting effects (>24 hours).²¹ Rupatadine also has an inhibitory effect on mast cell degranulation, eosinophil recruitment, and cytokine release in vitro.²¹

The efficacy and safety of rupatadine for the treatment of AR have been evaluated in phase 2 and phase 3 studies^{18,22,23};

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rupatadine, 10 and 20 mg, was significantly superior to placebo in reducing daily SAR-related symptoms and at least as effective as other established standard therapies. Similarly, its efficacy in the treatment of perennial AR was demonstrated. Rupatadine treatment was well tolerated, and at the recommended dose of 10 mg, it showed the most favorable risk-benefit balance.

The objective of the present placebo-controlled study was to evaluate the effects of 10 mg of rupatadine on grass pollen-induced nasal and nonnasal symptoms and nasal airflow in an allergen-exposure chamber. In a natural allergen exposure (eg, during the pollen period), the air concentration of allergenic particles is affected by a variety of factors related to (1) the variability in air allergen concentration, (2) allergen differences from location to location and from day to day at any single place, (3) the individual patient's exposure to allergen, and (4) the evaluation of allergic response to treatment.

The Vienna Challenge Chamber (VCC) offers an ideal system for studying the efficacy of rupatadine for the treatment of allergen-induced symptoms.²⁴ The major advantages of this system are the homogeneous and constant concentration of aeroallergen in the air, consistent with everyday allergen exposure during hay fever periods, and the possibility of performing quantitative and dynamic tests together with close monitoring and direct documentation of all findings.²⁵ In the VCC, patients could be challenged simultaneously under controlled conditions for several hours. Subjective and objective assessments, ie, evaluation of nasal and nonnasal symptom severity, nasal airflow, nasal secretion collection, and subjective "feeling of complaint" were performed online during exposure.

METHODS

Patients

The inclusion criteria were as follows: 18 to 45 years old, a body mass index of 18 to 30 (calculated as weight in kilograms divided by the square of height in meters), a history of SAR of at least 2 years, and sensitivity to grass pollen demonstrated by a positive response to skin prick testing and a positive radioallergosorbent test result at screening or during the previous 12 months. At screening, patients were exposed to grass pollen for 2 hours in the VCC to ensure that they had an adequate, measurable nasal allergic response. At entry into the VCC, eligible patients had no or mild nasal congestion (score ≤ 1), which increased to at least moderate congestion (score ≥ 2) during exposure. Nasal airflow had to decrease by at least 30% within 2 hours. The inclusion criteria also included no pregnancy or lactation; using an appropriate method of contraception; no clinically important abnormal physical findings; no clinically relevant abnormal laboratory values; no allergy or hypersensitivity to the study medication; no renal or hepatic impairment; no history of chronic nasal or upper respiratory tract symptoms or disorders other than AR; no history of nonallergic rhinitis, chronic

sinusitis, or severe bronchial asthma; no respiratory tract infection within 30 days; no participation in the evaluation of any drug within 3 months; adequate washouts for corticosteroids (depot, 90 days; systemic, 30 days; and dermatologic, 14 days), chromones (14 days), antihistamines (astemizole, 90 days; nasal and long-acting oral, 10 days; short-acting oral, 12–48 hours; and ocular, 3 days), decongestants (1–3 days), leukotriene inhibitors (10 days), herbal remedies (3 days), systemic antibiotics (14 days), anticholinergics (7 days), tricyclic antidepressants (28 days), ophthalmic nonsteroidal anti-inflammatory drugs (3 days), nasal-ophthalmic wash solutions, and immunotherapy (12 hours); and no maintenance immunotherapy for 24 hours before study dosing. No enrolled patients had concomitant asthma.

The study was performed outside the grass allergy season (the Vienna grass pollen period is approximately May 25 to July 25) to avoid bias due to individual seasonal allergic response at baseline. The study protocol was approved by the local ethics committee, and the Austrian health authorities were notified. All the patients provided written informed consent before enrollment and understood and complied with the requirements of the entire study.

Study Design

This was a randomized, double-blind, placebo-controlled, crossover trial. Patients were randomized to receive a 10-mg rupatadine tablet or identical placebo each morning for 8 consecutive days in 2 different periods separated by a wash-out interval of at least 14 days. During each study period, the last drug dose (day 8) was administered 60 minutes before stimulation with the pollen of *Dactylis glomerata* in the VCC. Study drugs were provided by J. Uriach y Compañía SA, Barcelona, Spain.

In the VCC, a dispersal system was used to maintain a uniform grass pollen concentration throughout the chamber (average pollen density of approximately 1,400 grains/m³), which was monitored every 5 minutes using a modified Burkard pollen trap. Ambient conditioned air was kept constant at 24°C and 40% humidity using a second air circuit. The chamber has an area of 21 m² and seats up to 24 patients separated from supervising staff by a polymethyl methacrylate screen; an intercom is used for communication. During the challenge sessions (2 hours at screening and 6 hours on day 8 of both study periods), every patient was monitored at short intervals. Subjective and objective assessments were performed online during exposure.

Assessments

Nasal and nonnasal allergen-induced symptom severity were self-evaluated at baseline and every 15 minutes during allergen exposure by giving a score of 0 to 3 for each symptom, where 0 indicated no symptoms; 1, mild (symptoms clearly present, well tolerated); 2, moderate (definite awareness of symptoms, bothersome but tolerable); and 3, severe (symptoms hard to tolerate, interfere with planned activities). Nasal symptoms were nasal congestion, nasal rhinorrhea, nasal

itching, and sneezing attacks; nonnasal symptoms were itching eyes, tearing eyes, eye redness, and itching of the ears and palate. The variables were rated as single symptom scores and as composite symptom scores, with the latter defined as (1) total nasal symptom scores (TNSSs), ie, the sum of the 4 nasal symptom scores; (2) total nonnasal symptom scores (TNNSSs), ie, the sum of the 4 nonnasal symptom scores; and (3) total symptom scores (TSSs), ie, the sum of the TNSS and the TNNSS. The primary efficacy variable of the study was the TNSS.

Nasal airflow was determined using active anterior rhinomanometry at a pressure difference of 150 Pa across the nasal passages (sum of the right and left nostril values) immediately before (baseline) and every 30 minutes during allergen exposure in the VCC at screening (2 hours) and on day 8 of each study period (6 hours). Nasal secretions were collected using sealed, preweighed packets of absorbent paper tissues. Patients cleared their noses using the tissues provided at baseline and whenever necessary during allergen exposure. Nasal secretion weights were calculated every 30 minutes. Overall subjective feeling of complaint was evaluated at baseline and every 15 minutes during allergen exposure using a 10-cm Huskisson visual analog scale ranging from 0 cm (no complaints) to 10 cm (very strong complaints).

The safety and general tolerability of the drug were based on records of adverse events (AEs) during the entire study and on the results of a full physical examination, including routine laboratory tests, performed at screening and at the end of the study. Vital signs (blood pressure, heart rate, and body temperature) were evaluated at screening, during the study, and at the final visit.

Statistical Methods

Sample size was calculated using the Stolley and Strom formula for clinical pharmacology studies,²⁶ based on type I error of 5% (2-tailed); type II error of 20%; the variability observed in previous studies, ie, SD = 2.8²⁶; and the requirement to detect a minimum difference of 1.32 in the primary variable (TNSS). According to the calculation, 36 patients were needed in the present study in crossover design. To compensate for possible nonevaluable patients, 45 individuals were enrolled.

Differences in allergen-induced symptom severity scores (nonparametric data) between treatments were compared at baseline and at 2 and 6 hours using the Friedman test applied to score distribution and the χ^2 test applied to score frequency distribution at $\alpha = .05$. For nasal airflow, nasal secretion weights, and overall feeling of complaint, the areas under the curve (AUCs) at 0 to 2 hours, 2 to 6 hours, and 0 to 6 hours during allergen exposure were calculated using validated software (Kinetica version 4.2; InnaPhase Corp, Philadelphia, PA). Mean changes from baseline for nasal airflow and feeling of complaint were calculated. Descriptive statistics of observed values, as well as AUCs and mean changes from baseline, were determined.

Nasal airflow, nasal secretion, and overall feeling of complaint AUCs and changes from baseline were evaluated using analysis of variance for a crossover design with factors of study drug, sequence, and period. Nonparametric tests were used when more appropriate. For the changes from baseline, time and time $\times$ treatment interactions were also evaluated. *P* values were calculated for the differences between rupatadine and placebo values. Comparisons were 2-sided ($\alpha = .05$). Statistical analyses were performed using a software program (SAS version 8.2 for Windows; SAS Institute Inc, Cary, NC). The evaluation of safety was based on the frequency of AEs and on the number of laboratory values falling outside the reference ranges. Vital signs after exposure vs baseline were evaluated using analysis of variance.

RESULTS

Of 46 patients screened, 45 were included in the study. One patient did not show a measurable response to aeroallergens during screening and was excluded. All 45 enrolled patients completed the study according to the protocol and were fully evaluated. Demographic data are summarized in Table 1.

Allergen-Induced Symptom Severity Scores

Baseline scores for subjective single nasal and nonnasal symptoms and baseline TNSSs, TNNSSs, and TSSs were similar for the 2 treatments, as confirmed by statistical results that showed no significant differences in the score distribution (Friedman test) and in the distribution of the frequency of scores (χ^2 test) (Table 2).

During exposure, mean scores for the 4 nasal symptoms, the 4 nonnasal symptoms, and the composite symptoms (TNSS, TNNSS, and TSS) were consistently lower for rupatadine treatment than for placebo use, starting from the first evaluation time, ie, at 15 minutes, to the end of the 6-hour challenge. Results of score frequencies for the 2 groups showed a distribution toward lower scores for the active treatment compared with placebo use (data not shown). Dif-

Table 1. Demographic Characteristics of the 45 Study Patients

	Treatment sequence 1*	Treatment sequence 2†	Total
Age, y			
Mean $\pm$ SD	25.35 $\pm$ 5.65	24.77 $\pm$ 3.91	25.10 $\pm$ 4.83
Range	20–45	18–33	18–45
Sex, No.			
M	1	3	4
F	22	19	41
Race, No.			
White	23	21	44
Black	0	1	1

* Treatment with 10 mg of rupatadine once daily for 8 days followed by 14 or more days of washout and then once-daily placebo use for 8 days.

† Treatment with placebo once daily for 8 days followed by 14 or more days of washout and then treatment with 10 mg of rupatadine once daily for 8 days.

Table 2. Summary of Individual and Composite Nasal and Nonnasal Symptom Scores*

Symptom and time	Rupatadine	Placebo	Friedman P value
Nasal Symptom Scores			
Nasal congestion			
0 h	0.1 ± 0.3	0.2 ± 0.4	NS
2 h	1.5 ± 0.8	1.9 ± 0.7	.002
6 h	1.7 ± 0.9	2.2 ± 0.7	.005
Nasal rhinorrhea			
0 h	0.2 ± 0.4	0.1 ± 0.3	NS
2 h	1.2 ± 0.8	1.9 ± 0.9	<.001
6 h	1.3 ± 0.9	2.0 ± 0.9	<.001
Nasal itching			
0 h	0.1 ± 0.3	0.1 ± 0.4	NS
2 h	1.1 ± 0.8	2.0 ± 0.9	<.001
6 h	1.1 ± 1.0	2.2 ± 0.9	<.001
Sneezing attacks			
0 h	0.1 ± 0.3	0.1 ± 0.4	NS
2 h	0.8 ± 0.7	1.7 ± 1.0	<.001
6 h	0.9 ± 0.9	1.9 ± 0.9	<.001
Nonnasal Symptom Scores			
Itching eyes			
0 h	0.0 ± 0.2	0.0 ± 0.2	NS
2 h	0.6 ± 0.8	1.4 ± 0.9	<.001
6 h	0.9 ± 1.0	1.5 ± 0.9	<.001
Tearing eyes			
0 h	0.0 ± 0.0	0.0 ± 0.0	†
2 h	0.3 ± 0.5	0.8 ± 1.5	.002
6 h	0.4 ± 0.6	0.8 ± 0.8	<.001
Eye redness			
0 h	0.0 ± 0.1	0.0 ± 0.1	NS
2 h	0.3 ± 0.5	0.8 ± 0.8	<.001
6 h	0.4 ± 0.8	0.8 ± 0.9	<.001
Itching ears and palate			
0 h	0.0 ± 0.2	0.1 ± 0.4	NS
2 h	0.4 ± 0.7	1.0 ± 1.0	.002
6 h	0.6 ± 0.8	0.9 ± 0.9	.005
Composite Symptom Scores			
Total nasal symptom score			
0 h	0.4 ± 1.1	0.5 ± 1.4	NS
15 min	2.9 ± 2.2	4.7 ± 2.7	.001
30 min	3.8 ± 2.5	6.5 ± 3.0	<.001
45 min	4.4 ± 2.4	7.3 ± 3.1	<.001
1 h	4.6 ± 2.6	7.4 ± 2.9	<.001
2 h	4.5 ± 2.5	7.5 ± 2.9	<.001
6 h	5.0 ± 3.2	8.2 ± 2.8	<.001
Total nonnasal symptom score			
0 h	0.1 ± 0.4	0.2 ± 0.6	NS
2 h	1.6 ± 2.0	4.0 ± 2.7	.002
6 h	2.2 ± 2.7	4.0 ± 2.8	<.001
Total symptom score			
0 h	0.5 ± 1.3	0.7 ± 1.8	NS
2 h	6.1 ± 3.9	11.5 ± 4.5	<.001
6 h	7.2 ± 5.2	12.2 ± 4.5	<.001

Abbreviation: NS, not significant.

* Data are given as mean ± SD.

† The P value is missing because identical score distributions were compared.

ferences in all individual and composite nasal and nonnasal symptom scores between treatments at 2 and 6 hours during VCC exposure were statistically significant, indicating that rupatadine treatment improved all individual and combined allergen-induced symptoms (Table 2). The most significant effects were seen for nasal rhinorrhea, nasal itching, and sneezing attacks ($P < .001$ for all), although all the other symptoms were significantly reduced with active treatment compared with placebo use as well, including nasal congestion (Fig 1).

Differences in TNSSs between treatments were significant at all evaluation times, ie, 30 minutes, 2 hours, and 6 hours ($P < .001$), with reduced total nasal symptoms in favor of rupatadine treatment. At 15 minutes from the beginning of VCC exposure, significantly lower TNSSs for rupatadine vs placebo were already observed ($P = .001$), indicating a rapid onset of action of the active drug (Fig 2).

Nasal Airflow and Secretion

Mean nasal airflow values at baseline were similar for the rupatadine and placebo treatments, although considerable interindividual variation was observed (Table 3). During VCC exposure, nasal airflow decreased for both treatments. However, nasal airflow after rupatadine treatment remained slightly higher than after placebo use during most of the challenge, indicating slightly less nasal congestion after dosing with the active drug. Two hours after allergen exposure, mean changes from baseline were less substantial for rupatadine treatment than for placebo use. However, at the end of the VCC challenge, mean changes from baseline were similar for the 2 treatments, and no significant difference between treatments was observed. Results of statistical analysis showed that differences in AUC values between the 2 treatment groups were not significant at any of the times considered (Table 3).

Mean secretion weights during the 6 hours of VCC exposure after multiple treatments with rupatadine were consistently lower than after placebo treatment. Statistical analysis using the no ties–Friedman test applied to the AUC variables showed that differences between treatments were statistically significant at all times analyzed (Table 3).

Subjective Feeling of Complaint

At entry into the VCC, mean overall subjective feeling of complaint was very low for all the patients, with no differences between treatments. The rupatadine and placebo groups showed an increased feeling of complaint during exposure, starting from the first evaluation time (15 minutes). However, the rupatadine group showed lower scores than the placebo group, indicating better overall tolerability during allergen exposure. Differences between treatments in mean changes from baseline (2 hours and 6 hours) and in AUC values (0–2 hours, 2–6 hours, and 0–6 hours) were statistically significant (Table 3).

Safety

No serious AEs occurred during the study. The AE rates were very low and did not differ between the rupatadine (1/45

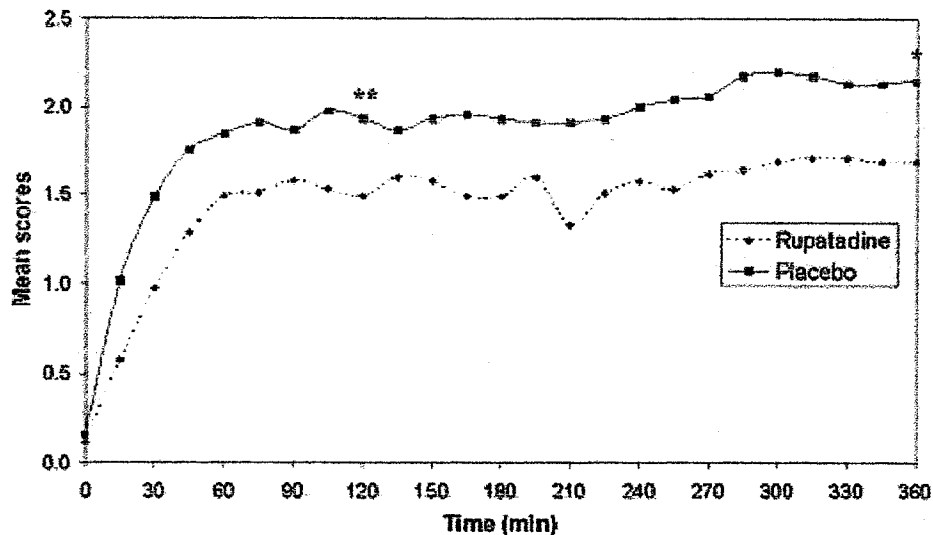


Figure 1. Mean nasal congestion scores at each evaluation time during allergen exposure in the Vienna Challenge Chamber for rupatadine and placebo treatments. Statistical analysis was performed at baseline and at 2 and 6 hours during allergen exposure. Asterisk indicates $P < .005$; double asterisk, $P < .002$.

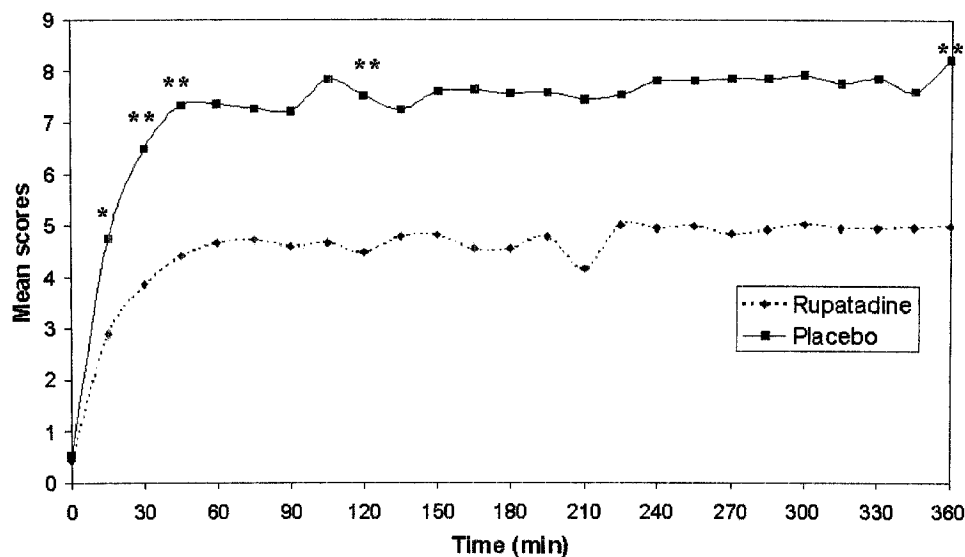


Figure 2. Mean total nasal symptom scores at each evaluation time during allergen exposure in the Vienna Challenge Chamber for rupatadine and placebo treatments. Statistical analysis was performed at baseline, at 15 and 30 minutes, and at 1, 2, and 6 hours during allergen exposure. Asterisk indicates $P < .001$; double asterisk, $P < .001$.

[2%]) and placebo (2/45 [4%]) treatments. One patient in the rupatadine group reported cough, and 1 each in the placebo group reported headache and tiredness. The AE reported during rupatadine treatment, ie, cough, was not related to the study drug and occurred 1 day before VCC challenge. All AEs were of either moderate or mild intensity; their severity was judged not to be clinically relevant, and all resulted in complete recovery. No clinically relevant effects of treatment

or VCC exposure on vital signs and laboratory values were observed.

DISCUSSION

The results of the present study show that in patients with allergen-induced rhinitis, the administration of rupatadine is associated with highly significant relief of allergic symptoms. Rupatadine treatment produced a greater reduction than placebo

Table 3. Summary of Nasal Airflow, Nasal Secretion Weights, and Overall Feeling of Complaint*

Variable	Time, h	Rupatadine	Placebo	P value
Nasal airflow, mL/s				
Observed value	0	1,125.4 ± 305.0	1,126.0 ± 345.3	NA
	2	680.0 ± 296.1	639.4 ± 308.3	NA
	6	634.0 ± 283.5	637.4 ± 267.6	NA
AUC	0–2	92,718.3 ± 31,501.6	86,658.7 ± 33,291.0	.12
	2–6	162,558.7 ± 65,336.5	150,194.0 ± 59,598.5	.10
	0–6	255,277.0 ± 93,601.5	236,852.7 ± 90,688.6	.09
Nasal secretion weights, g				
Observed value	0	NA	NA	NA
	2	1.4 ± 1.4	3.1 ± 2.5	NA
	6	1.4 ± 1.4	2.2 ± 1.5	NA
AUC	0–2	154.5 ± 168.4	303.0 ± 227.2	<.001
	2–6	308.8 ± 310.9	598.7 ± 388.7	<.001
	0–6	463.9 ± 461.3	901.9 ± 592.2	<.001
Overall feeling of complaint measured by VAS, cm				
Observed value	0	4.9 ± 5.6	7.6 ± 11.2	NA
	2	26.2 ± 19.0	46.8 ± 21.9	NA
	6	32.7 ± 24.9	53.4 ± 23.2	NA
AUC	0–2	2,525.8 ± 1,712.1	4,373.5 ± 2,171.2	<.001
	2–6	7,173.3 ± 4,708.6	11,833.5 ± 5,035.6	<.001
	0–6	9,699.2 ± 6,242.9	16,207.0 ± 6,889.6	<.001

Abbreviations: AUC, area under the curve; NA, not analyzed; VAS, visual analog scale.

* Data are given as mean ± SD.

in the severity of all the symptoms evaluated, and these reductions were statistically significant at all the evaluation times.

In general, antihistamines are considered to be less effective against nasal obstruction than against other allergen-induced symptoms.⁴ Herein, nasal obstruction was evaluated subjectively as the symptom of nasal congestion and objectively, using rhinomanometry, as decreased nasal airflow. Although subjective nasal congestion was significantly reduced with rupatadine therapy compared with placebo use, the difference between treatments in nasal airflow variables was not significant.

Similar results were observed in a VCC trial²⁷ performed with cetirizine, 10 mg once daily, vs fexofenadine, 120 mg once daily, in which the 2 active treatments produced significantly less nasal congestion symptoms than placebo, whereas nasal airflow was not significantly improved. However, the sample size of the present study was powered to detect a difference between treatments based on the primary variable of TNSS (see the “Statistical Methods” subsection). Owing to the high variability in the values of nasal airflow already observed at baseline, many more patients would be needed to detect a statistically and clinically significant difference between treatments. On the other hand, in a recent clinical trial²⁴ in patients with SAR, rupatadine therapy did not improve nasal congestion during the allergy season. Allergic nasal obstruction is caused by inflamed and swollen mucosa, with engorgement of sinusoidal capacitance vessels, rhinorrhea, and increased mucus production.^{28,29}

In addition to statistically reducing nasal congestion and rhinorrhea symptoms, rupatadine treatment significantly re-

duced secretion weights throughout the allergen exposure challenge. Better subjective overall tolerability during allergen exposure after rupatadine treatment compared with placebo use was also observed. Taken together, the results demonstrate the reproducibility of assessments made in the VCC, which is an increasingly important factor for experimental conditions, as shown in previous studies.^{25,28–31}

These results give a preliminary suggestion of the potential decongestant activity of rupatadine, which, however, needs to be further investigated compared with other second-generation antihistamines.³² The reason that rupatadine demonstrated benefits in terms of subjective measures of nasal congestion might be a function of its potent H₁ receptor antagonism allied with inhibition of allergic inflammatory mediators.³² Although these in vitro data are interesting, their significance remains to be determined in humans. Rupatadine previously showed a good efficacy profile in terms of controlling SAR symptoms such as rhinorrhea and sneezing.^{24,33}

Rupatadine showed rapid onset of action, as indicated by statistically significantly lower TNSSs compared with placebo, starting from the first evaluation time during exposure (15 minutes) and, therefore, 75 minutes after drug administration, in accordance with the general onset of action expected with common antihistamines, ie, 1 to 3 hours after drug intake. A clinical study²⁸ performed with loratadine and levocetirizine on patients with SAR exposed to grass pollen in the VCC for 6 hours on 2 consecutive days and administered the study drugs 2 hours after the beginning of challenge reported onset of action of 45 and 75 minutes after loratadine and levocetirizine intake, respectively. The long duration of

action of rupatadine was confirmed by the continued significantly lower scores at the last evaluation time.

In conclusion, we demonstrated that rupatadine, 10 mg once daily, is effective and well tolerated in patients with allergen-induced rhinitis exposed to allergens in a controlled chamber and could represent a safe and effective treatment option for patients with AR. The present study, furthermore, confirmed the value of the VCC as an accurate method for the controlled exposure of patients to specific allergens, as also demonstrated by previous clinical trials.²⁷⁻³¹

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